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Serial No.: 10/030,330

Confirmation No.: 4105

Filed: October 19, 2001

For: A POLYPEPTIDE HAVING AMIDOLYTIC ACTIVITY FOR A SERPIN

Remarks

The Office Action mailed July 2, 2003, has been received and reviewed. Claims 17 and 30 having been canceled, claims 1, 8, 11, 14, 16, 18-27, and 29 having been amended, and claims 31-38 having been added, the pending claims are claims 1-16, 18-29, and 31-38.

Claims 1, 8, 11, and 27 have been amended to recite that the "polypeptide comprises an amino acid sequence having a percentage amino acid identity of greater than 37% to that of SEQ ID NO: 1," which is supported, for example, by originally filed claim 17, now canceled. Claims 14, 19, 25, and 26 have been amended to recite that the polypeptide "has amidolytic activity for cleavage of a nondenatured serpin at a reactive site loop region of the serpin," which is supported, for example, by originally filed claim 11. Claim 14 has also been rewritten in independent form. Claim 16 has been amended to recite that "the polypeptide further nonspecifically cleaves the serpin in a denaturing environment," which is supported by the specification at, for example, page 12, lines 18-30. Claims 18 and 20 have been amended to delete the recitation of "an active analog or an active fragment thereof." Claims 21-23 and 25-26 have been amended to delete the recitation of nucleic acid "fragment." Claims 21-22 and 26 have been amended to recite that "the encoded polypeptide comprises an amino acid sequence having a percentage amino acid identity of greater than 37% to amino acid 148 to amino acid 843 of SEQ ID NO: 1," which is supported, for example, by originally filed claim 19. Claims 21 and 22 have been amended to recite that "the nucleic acid has at least about 50% identity with SEQ ID NO:2," which is supported by the specification at, for example, page 21, lines 31-32. Claims 22 and 23 have been amended to incorporate a hybridization recitation which is supported, for example, by originally filed claim 26. Claim 23 has been amended to delete the recitation that the polypeptide "is isolated from *Porphyromonas gingivalis*," which is now recited in dependent claim 31. Claim 24 has been rewritten in independent form. Claim 26 has been amended by deleting the recitation that "at least about 15 nucleotides of the complement hybridize."

New claims 31 and 32 are generally supported by the specification and claims (e.g., claim 23). New claims 33 and 35 are supported, for example, by originally filed claims 8

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and 17, and the specification at, for example, page 14, lines 4-14. New claim 34 is supported, for example, by originally filed claims 8, 17, and 27. New claims 36 and 37 are generally supported by the specification (e.g., page 4, lines 30-32). Claim 38 is supported by the specification at, for example, page 11, lines 28-29.

Reconsideration and withdrawal of the rejections are respectfully requested.

Restriction Requirement

Applicants thank the Examiner for reconsidering and withdrawing the Restriction Requirement under 35 U.S.C. §121.

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claim 16 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner alleged that the phrase "which cleaves a target polypeptide nonspecifically" is ambiguous. Applicants respectfully traverse the rejection.

Applicants respectfully submit that it would be clear to one of skill in the art that a target polypeptide "includes any denatured polypeptide and/or a native polypeptide, i.e., nondenatured, that contains at least one exposed contiguous amino acid region, such as a random coil as determined for example, by x-ray crystallography, that is susceptible to cleavage" (e.g., specification at page 7, lines 1-4).

However, in the interest in expediting the prosecution of the present application, claim 16 has been amended to recite that "the polypeptide further nonspecifically cleaves the serpin in a denaturing environment," and the rejection has been obviated. Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §112, second paragraph.

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Rejection under 35 U.S.C. §112, First Paragraph***Lack of Written Description***

The Examiner rejected claims 1-23 and 25-29 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 17 having been canceled, and claims 1, 8, 11, 14, 16, 18-23, 25-27, and 29 having been amended, Applicants respectfully traverse the rejection.

To meet the written description requirement of 35 U.S.C. §112, first paragraph, the application "must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, i.e., what is now claimed." M.P.E.P. §2163. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

Applicants respectfully submit that the presently pending claims (as amended) meet the written description requirement of 35 U.S.C. §112, first paragraph, for at least the reasons recited herein below.

First, independent claims 18 and 20 recite polypeptides having specific sequences. Applicants respectfully submit that claims 18 and 20 reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Second, independent claims 1, 8, 11, 14, 19, 21-23, 25-27, and 29 all recite polypeptides having the recited amidolytic activity (i.e., function). Further, in addition to function, independent claims 1, 8, 11, 14, 19, 21-23, 25-27, and 29 all recite structural characteristics.

Specifically, claims 22-23 and 26 all recite hybridization to SEQ ID NO:2; claims 1, 8, 11, 14, 19, 21-22, 25-27, and 29 all recite polypeptide homology (i.e., percentage amino

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acid identity) to recited sequences; and claims 21-22 recite nucleic acid homology (i.e., % identity) with SEQ ID NO:2. Notably, in addition to function, claim 21 recites both polypeptide homology and nucleic acid homology; claim 26 recites both hybridization to SEQ ID NO:2 and polypeptide homology; and claim 22 recites hybridization to SEQ ID NO:2, nucleic acid homology, and polypeptide homology.

Moreover, in some embodiments of the present invention, the claims recite *Porphyromonas gingivalis*, the organism from which the polypeptide is isolated (e.g., claims 3, 10-11, 14, and 28 (and new claims 31-32).

Finally, in preferred embodiments of the present invention, the claims recite physical and/or chemical properties of the polypeptide including, for example, a polypeptide that is a cysteine proteinase (e.g. claim 4), or has a molecular weight of about 70 kD to about 80 kD (e.g., claims 5 and 13).

Thus, Applicants respectfully submit that claims 1-16, 18-23, and 25-29 recite appropriate combinations of structure, physical and/or chemical properties, and functional characteristics to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §112, first paragraph, for lack of written description.

Lack of Enablement

The Examiner rejected claims 1-23 and 25-29 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 17 having been canceled, and claims 1, 8, 11, 14, 16, 18-23, 25-27, and 29 having been amended, Applicants respectfully traverse the rejection.

"A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing

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and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." M.P.E.P. §2164.04. "As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." M.P.E.P. §2164.01(b). "For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be *used* in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not *use* the genus as a whole without undue experimentation." M.P.E.P. §2164.02, paragraph entitled "WORKING EXAMPLES AND A CLAIMED GENUS" (emphasis added).

The specification clearly describes methods of making the isolated polypeptides (e.g., page 11, line 20 to page 13, line 13; page 17, line 5 to page 18, line 16) and isolated nucleic acids (e.g. page 19, line 7 to page 22, line 2) recited in the claims. Although not required, Applicants have even provided working examples of isolated nucleic acids and isolated polypeptides (e.g. page 25, line 25 to page 42, line 30). Further, the specification provides methods of using the isolated polypeptides (e.g., page 23, line 21 to page 25, line 13) and isolated nucleic acids (e.g., page 22, line 3 to page 23, line 20). Notably, the Examiner has not provided any reason to doubt the objective truth of the disclosure provided in the specification.

Furthermore, independent claims 1, 8, 11, 14, 18-22, 25-27, and 29 describe isolated polypeptides by reciting physical and/or chemical properties including, for example, specific sequences (e.g., independent claims 18 and 20) and/or structural identity (e.g. independent claims 1, 8, 11, 14, 19, 21-22, 25-27, and 29), as further described herein above under the remarks to the rejection based on lack of written description. Similarly, independent claims 21-23 and 26 describe isolated nucleic acids by reciting physical and/or chemical

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properties including, for example, hybridization conditions (e.g., independent claims 22-23 and 26) and/or structural identity (e.g. independent claims 21-22), as further described herein above under the remarks to the rejection based on lack of written description. Independent claims 1, 8, 11, 14, 19, 21-23, 25-27, and 29 further recite polypeptides having function (e.g., amidolytic activity").

Further, Applicants respectfully submit that one of skill in the art, using the disclosure provided in the specification (including the working examples), would be able to make and use the entire scope of the invention as recited in the presently pending claims. For example, the specification provides guidance to one of skill in the art in selecting amino acids for substitution into the encoded polypeptide (e.g., page 16, line 4 to page 17, line 4). Further, Applicants respectfully submit that one of skill in the art, in view of the present specification, would be enabled to select appropriate amino acids in the polypeptide as candidates for substitution.

Moreover, the specification provides one of skill in the art exemplary methods of assaying isolated polypeptides for amidolytic activity (e.g., page 12, lines 2-17; page 18, lines 11-16; page 26, line 26 to page 27, line 24).

Applicants respectfully request that the rejections under 35 U.S.C. §112, first paragraph, for lack of enablement, be reconsidered and withdrawn.

Rejection under 35 U.S.C. §102

The Examiner rejected claim 30 under 35 U.S.C. §102 as being anticipated by Burdavari et al. (THE MERCK INDEX, pg. 932, 1996). Claim 30 having been canceled, the rejection is rendered moot. Applicants respectfully request that the rejection be withdrawn.

The Examiner rejected claims 21-23 and 25-26 under 35 U.S.C. §102(e) as being anticipated by U.S. Pat. No. 6,444,799 (Ross).

Ross has a filing date of December 23, 1998. A Declaration under 37 C.F.R. §1.131 is being submitted concurrently herewith in which Applicants James Travis, Jan S. Potempa, and Daniel C. Nelson swear that before December 18, 1998, they reduced to practice

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the invention as recited in originally filed claims 1-23 and 25-29. The reduction to practice is evidenced, for example, by accompanying Exhibit A (Nelson et al., "Purification and Characterization of a Novel Cysteine Proteinase (Periodontain) from *Porphyromonas gingivalis*," *J. Biological Chem.*, 274:12245-12251 (1999), which was submitted for publication on or before December 11, 1998). Thus, the Declaration under 37 C.F.R. §1.131 antedates Ross. Applicants respectfully request that Ross be removed as a reference and that any rejections under 35 U.S.C. §102(e) based on Ross be withdrawn.

Rejection under 35 U.S.C. §103

The Examiner rejected claims 1-20 and 29 under 35 U.S.C. §103(a) as being unpatentable over U.S. Pat. No. 6,444,799 (Ross). The Examiner rejected claims 27 and 28 under 35 U.S.C. §103(a) as being unpatentable over U.S. Pat. No. 6,444,799 (Ross), and Madden et al. (Inf. Imm.63:238-247, 1995) in view of Chen et al. (*J. Biol. Biochem.* 267:18896-18901, 1992) and Nelson et al. (*Analyt. Biochem.* 260:230-236, 1998).

As described herein above, the accompanying Declaration under 37 C.F.R. §1.131 antedates Ross. Applicants respectfully request that Ross be removed as a reference and that any rejections under 35 U.S.C. §103(a) based on Ross be withdrawn.

Objection to the Claims

The Examiner objected to claim 24 as being dependent upon a rejected base claim, but indicated that claim 24 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants have rewritten claim 24 in independent form and respectfully request that claim 24 as amended be considered and passed on to allowance.

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New Claims

New claims 31 and 32 depend from claims 23 and 25, respectively. Applicants respectfully submit that claims 31 and 32 are patentable for at least the reasons recited herein above for the patentability of claims 23 and 25.

New claims 33 and 34 recite methods of inhibiting the amidolytic activity of a polypeptide, wherein the polypeptide has amidolytic activity for cleavage of a nondenatured serpin at a reactive site loop region of the serpin, and wherein the polypeptide comprises an amino acid sequence having a percentage amino acid identity of greater than 37% to that of SEQ ID NO: 1. Applicants respectfully submit that new claims 33 and 34 are patentable for at least the reasons recited herein above for the patentability of, for example, claims 1, 8, 11, 27, and 29.

New claim 35 recites a kit including an agent and instructions for combining the agent with a polypeptide, wherein the polypeptide has amidolytic activity for cleavage of a nondenatured serpin at a reactive site loop region of the serpin, and wherein the polypeptide comprises an amino acid sequence having a percentage amino acid identity of greater than 37% to that of SEQ ID NO: 1. Applicants respectfully submit that new claim 35 is patentable for at least the reasons recited herein above for the patentability of, for example, claims 1, 8, 11, 27, and 29.

New claim 36 recites "[a]n isolated nucleic acid encoding a polypeptide comprising SEQ ID NO:1;" new claim 37 recites "[a]n isolated nucleic acid encoding a polypeptide consisting of SEQ ID NO:1;" and new claim 38 recites "[a]n isolated polypeptide comprising an amino acid sequence represented by amino acid 148 to amino acid 629 of SEQ ID NO:1." Applicants respectfully submit that claims 36-38 are patentable for at least the reasons recited herein above for the patentability of, for example, claims 18 and 20.

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Summary

It is respectfully submitted that all the pending claims are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for

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CERTIFICATE UNDER 37 CFR §1.8:

The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Assistant Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 3rd day of November, 2003, at 2:05 p.m. (Central Time).

By: Name: Rachel Englandi-Cabala